

Replace the paragraph beginning at page 9, line 25, with the following rewritten paragraph:

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--As discussed herein, the blocking agents used in methods of the invention are not limited to antibodies or antibody derivatives, but may be other molecules, e.g., soluble forms of other proteins which bind VLA-4, e.g., the natural binding proteins for VLA-4. These binding agents include soluble VCAM-1 or VCAM-1 peptides, VCAM-1 fusion proteins, bifunctional VCAM-1/Ig fusion proteins, fibronectin, fibronectin having an alternatively spliced non-type III connecting segment, and fibronectin peptides containing the amino acid sequence EILDV (SEQ ID NO:16) or a similar conservatively substituted amino acid sequence. These binding agents can act by competing with the cell-surface binding protein for VLA4 or by otherwise altering VLA-4 function. For example, a soluble form of VCAM-1 (see, e.g., Osborn et al. 1989 [18]) or a fragment thereof may be administered to bind to VLA-4, and preferably compete for a VLA-4 binding site, thereby leading to effects similar to the administration of anti-VLA-4 antibodies. Soluble VCAM-1 fusion proteins can be used in the methods described herein. For example, VCAM-1, or a fragment thereof which is capable of binding to VLA-4 antigen on the surface of VLA-4 bearing cells, e.g., a fragment containing the two N-terminal domains of VCAM-1, can be fused to a second peptide, e.g., a peptide which increases the solubility or the *in vivo* life time of the VCAM-1 moiety. The second peptide can be a fragment of a soluble peptide, preferably a human peptide, more preferably a plasma protein, or a member of the immunoglobulin super family. In particularly preferred embodiments, the second peptide is IgG or a portion or fragment thereof, e.g., the human IgG1 heavy chain constant region. A particularly preferred fusion protein is the VCAM 2D-IgG fusion.

Replace the paragraph beginning at page 10, line 35, with the following rewritten paragraph:

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--In another aspect the invention features a chimeric molecule which includes: (1) a VLA-4 targeting moiety, e.g., a VCAM-1 moiety capable of binding to VLA-4 antigen on the surface of VLA-4 bearing cells; (2) optionally, a second peptide, e.g., one which increases solubility or *in vivo* life time of the VLA-4 targeting moiety, e.g., a member of the

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immunoglobulin super family or fragment or portion thereof, e.g., a portion or a fragment of IgG, e.g., the human IgG1 heavy chain constant region, e.g., C<sub>H</sub>2 and C<sub>H</sub>3 hinge regions; and (3) a toxin moiety. The VLA-4 targeting moiety can be any naturally occurring VLA-4 ligand or fragment thereof, e.g., a VCAM-1 peptide, fibronectin, fibronectin having an alternatively spliced non-type III connecting segment, and fibronectin peptides containing the amino acid sequence EILDV (SEQ ID NO:16) or a similar conservatively substituted amino acid sequence. A preferred targeting moiety is a soluble VCAM-1 fragment, e.g., the N-terminal domains 1 and 2 of the VCAM-1 molecule. The toxin moiety can be any agent which kills or inactivates a cell when the toxin is targeted to the cell by the VLA-4 targeting moiety. Toxin moieties include: cytotoxic peptide moieties, e.g., Diphtheria toxin A, *Pseudomonas* Exotoxin, Ricin A, Abrin A, *Schigella* toxin, or Gelonin; radionucleotides; and chemotherapeutic agents.

Replace the paragraph beginning at page 16, line 21, with the following rewritten paragraph:

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In order to isolate a cDNA copy of the human IgG1 heavy chain region, RNA was prepared from COS7 cells which has been transiently transfected by the plasmid VCAM1-IgG1 (also known as pSAB133). Construction of plasmid VCAM1-IgG1 is described in PCT patent application WO 90/13300. The RNA was reverse transcribed to generate cDNA using reverse transcriptase and random hexamers as the primers. After 30 min. at 42°C, the reverse transcriptase reaction was terminated by incubation of the reaction at 95°C for 5 min. The cDNA was then amplified by PCR (Polymerase Chain Reaction, see, e.g., Sambrook et al., Molecular Cloning, Vol. 3, pp. 14.1-14.35 (Cold Spring Harbor; 1989) [29]) using the following kinased primers: 370-31:

5'TCGTC GAC AAA ACT CAC ACA TGC C (SEQ ID NO:6)

Asp Lys Thr His Thr Cys (SEQ ID NO:14)

which contains a Sall site, and 370-32 (SEQ ID NO: 7):

5' GTAAATGAGT GCGGCGGCCG CCAA,

which encodes the carboxy terminal lysine of the IgG1 heavy chain constant region, followed by a NotI site.

Replace the paragraph beginning at page 17, line 19, with the following rewritten paragraph:

The plasmid pSAB142 was constructed as follows. cDNA prepared from COS cells transfected with pSAB133 (as described in the previous section) was subjected to PCR amplification using oligonucleotides 370-01 and 370-29. Oligonucleotide 370-01 includes a NotI site and the nucleotides corresponding to amino acids 1 through 7 of the VCAM-1 signal sequence:

5' GAGCTCGAGG CGGCCGCACC ATG CCT GGG AAG ATG GTC GTG (SEQ ID NO:9)  
Met Pro Gly Lys Met Val Val (SEQ ID NO:15)

Oligonucleotide 370-29 corresponds to the VCAM-1 amino acids 214-219 and includes a SalI site (SEQ ID NO: 10):

5' AA GTC GAC TTG CAA TTC TTT TAC

The amplified DNA fragment was ligated to the vector fragment of pNN03, cleaved by EcoRV.